

CLAIMS

1. A method of screening for small organic compounds that inhibit the interaction of GAGs with GAG specific ECAMs, the method comprising the steps of:
 - a. contacting a GAG with an ECAM in the presence of at least one small organic compound; and
 - b. measuring the amount of the GAG bound to the ECAM or the amount of the ECAM bound to the GAG, wherein a significant decrease in GAG-ECAM binding in the presence of the compound as compared to GAG-ECAM binding in the absence of said compound identifies the compound as inhibitor compound inhibiting GAG-ECAM interaction.
2. A method of identifying small organic compounds that inhibit the interaction of GAGs with GAG specific ECAMs, the method comprising the steps of:
 - a. contacting a GAG with at least one small organic compound;
 - b. removing of unbound organic compound;
 - c. adding an ECAM; and
 - d. measuring the amount of the GAG bound to the ECAM or the amount of the ECAM bound to the GAG, wherein a significant decrease in GAG-ECAM binding for the GAG contacted with the organic compound as compared to GAG-ECAM binding for said GAG not contacted with the compound identifies said compound as inhibitor compound inhibiting GAG-ECAM interaction.
3. The method according to claims 1 and 2, wherein the GAG is selected from the group consisting of heparan sulfate (HS-GAG), heparin, chondroitin sulfate, dermatan sulfate, keratan sulfate, derivatives and fragments thereof.
4. The method according to claim 3, wherein the GAG is heparan sulfate (HS-GAG) or heparin.
5. The method according to claims 1 and 2 wherein the GAG is a part of a proteoglycan.
6. The method according to claim 5 wherein the proteoglycan is heparan-sulfate proteoglycan (HS-PG).
7. The method according to claims 1 and 2 wherein the ECAM is selected from the group consisting of selectins, integrins, fibronectin, and cytokines.
8. The method according to claim 7 wherein the ECAM is L-selectin or P-selectin.
9. The method according to claims 1 and 2 wherein the ECAM is a fusion protein.

10. The method according to claims 1 and 2, wherein the GAG or the ECAM are tagged or labeled.
11. The method according to claim 10 wherein the label is selected from the group consisting of a dye, a fluorescent dye, a chemoluminescent agent, or a radioactive agent.
12. The method according to claim 10 wherein the ECAM is tagged by an antibody.
13. A compound identified according to any of claims 1-12.
14. A pharmaceutical composition comprising as an active ingredient an inhibitor compound capable of inhibiting the interaction of GAGs with GAG specific ECAMs, the compound identified by a screening method comprising the steps of:
 - a. contacting a GAG with an ECAM in the presence of at least one small organic compound; and
 - b. measuring the amount of the GAG bound to the ECAM or the amount of the ECAM bound to the GAG, wherein a significant decrease in GAG-ECAM binding in the presence of the compound as compared to GAG-ECAM binding in the absence of said compound identifies the compound as inhibitor compound inhibiting GAG-ECAM interaction, further comprising a pharmaceutically acceptable diluent or carrier.
15. A pharmaceutical composition comprising as an active ingredient an inhibitor compound capable of inhibiting the interaction of GAGs with GAG specific ECAMs, the compound identified by a screening method comprising the steps of:
 - a. contacting a GAG with a small organic compound;
 - b. removing of unbound organic compound;
 - c. adding an ECAM; and
 - d. measuring the amount of the GAG bound to the ECAM or the amount of the ECAM bound to the GAG, wherein a significant decrease in GAG-ECAM binding for the GAG contacted with the organic compound as compared to GAG-ECAM binding for said GAG not contacted with the compound identifies said compound as inhibitor compound inhibiting GAG-ECAM interaction, further comprising a pharmaceutically acceptable diluent or carrier.
16. The pharmaceutical composition according to claims 14 and 15 wherein the GAG is selected from the group consisting of heparan sulfate (HS-GAG), heparin, chondroitin sulfate, dermatan sulfate, keratan sulfate, derivatives and fragments

thereof.

17. The pharmaceutical composition according to claims 14 and 15 wherein the ECAM is selected from the group consisting of selectins, integrins, fibronectin, and cytokines.
- 5 18. The pharmaceutical composition according to claim 17 wherein the selectin is L-selectin or P-selectin.
19. A method for inhibiting cell adhesion or cell migration comprising the step of exposing a cell to a small organic compound, said compound interacts with at least one GAG in an amount sufficient for preventing the interactions of the GAG with
- 10 at least one GAG specific ECAM.
20. The method according to claim 19 wherein cell adhesion or cell migration is inhibited in vitro.
21. The method according to claim 19 wherein cell adhesion or cell migration is inhibited in vivo.
- 15 22. The method according to claim 19 wherein the GAG is selected from the group consisting of heparan sulfate (HS-GAG), heparin, chondroitin sulfate, dermatan sulfate, keratan sulfate, derivatives and fragments thereof.
23. The method according to claim 22 wherein the GAG is heparan sulfate (HS-GAG) or heparin.
- 20 24. The method according to claim 19 wherein the GAG is a part of a proteoglycan.
25. The method according to claim 24 wherein the proteoglycan is heparan-sulfate proteoglycan (HS-PG).
26. The method according to claim 19 wherein the GAG specific ECAM is selected from the group consisting of selectins, integrins, fibronectin, and cytokines.
- 25 27. The method according to claim 26 wherein the GAG specific ECAM is P-selectin or L-selectin.
28. A method for modulating anticoagulant activity of glycosaminoglycans in a subject comprising the step of administering a therapeutically effective amount of a pharmaceutical composition according to any of claims 14 and 15, thereby
- 30 modulating the anticoagulant activity of glycosaminoglycans.
29. The method according to claim 28, wherein the glycosaminoglycan is heparin.
30. A method for the treatment or prevention of a condition, process, or a disorder related to cell adhesion or migration in a subject comprising the step of administering to a subject in need thereof a pharmaceutical composition

comprising as an active ingredient a therapeutically effective amount of a small organic compound, said compound inhibits the interaction of at least one GAG with at least one GAG specific ECAM, thereby preventing cell adhesion or cell migration mediated by the GAG.

5 31. The method according to claim 30 wherein the process, condition, or disorder related to cell adhesion or migration is selected from the group consisting of inflammatory processes, autoimmune processes, cancer, cancer metastasis, atherosclerosis, and platelet-mediated pathologies.

10 32. The method according to claim 31 wherein the inflammatory process is selected from the group consisting of septic shock, wound associated sepsis, post-ischemic leukocyte-mediated tissue damage, reperfusion injury, frost-bite injury, shock, acute leukocyte-mediated lung injury, adult respiratory distress syndrome, acute pancreatitis, liver cirrhosis, uveitis, asthma, transplantation rejection, graft versus host disease, traumatic shock, stroke, traumatic brain injury, nephritis, acute and
15 chronic inflammation, atopic dermatitis, psoriasis, and inflammatory bowel disease.

20 33. The method according to claim 31 wherein the autoimmune process is selected from the group consisting of rheumatoid arthritis, multiple sclerosis, systemic lupus erythematosus, Hashimoto's thyroiditis, Grave's disease, Myasthenia gravis, insulin resistance, and autoimmune thrombocytopenic purpura.

34. The method according to claim 31 wherein the cancer is leukemia.

25 35. The method according to claim 31 wherein the disease related to cell adhesion or cell migration is selected from the group consisting of bone degradation, restenosis, eczema, osteoporosis, and osteoarthritis and wound healing.